INTELLECTUAL PROPERTY **INDIA**

सत्यमेव जयते

GOVERNMENT OF INDIA
MINISTRY OF COMMERCE & INDUSTRY
PATENT OFFICE, DELHI
BOUDHIK SAMPADA BHAWAN,
PLOT NO. 32, SECTOR – 14,
NEW DELHI - 110 075.

I, the undersigned being an officer duly authorized in accordance with the provision of the Patent Act, 1970 hereby certify that annexed hereto is the true copy of the ***Application*** *and* ***Complete Specification*** *filed in connection with Application for Patent No.****1394/Del/2003*** *dated* ***12th November 2003.***

Witness my hand this 20th day of September 2005.

(P.K. PATNI)
Deputy Controller of Patents & Designs

FORM 1 1594 DEL 03

THE PATENTS ACT, 1970 12 NOV 2003
(39 of 1970)

APPLICATION FOR GRANT OF A PATENT
(See Sections 5(2), 7, 54 and 135; and rule 39)

1 We, **RANBAXY LABORATORIES LIMITED**, a Company incorporated under the Companies Act, 1956, Corporate Office at 19, Nehru Place, New Delhi - 110 019, India

2. hereby declare –

(a) that we are in possession of an invention titled **"IBUPROFEN-CONTAINING SOFT GELATIN CAPSULES"**

(b) that the Complete Specification relating to this invention is filed with this application.

(c) that there is no lawful ground of objection to the grant of a patent to us.

3. Further declare that the inventors for the said invention are

a. AJAY KUMAR SINGLA
b. INDERDEEP SINGH BHATIA
c. SANJEEV SETHI

of Ranbaxy Laboratories Limited, Plot No. 20, Sector-18, Udyog Vihar Industrial Area, Gurgaon 122001 (Haryana), India, all Indian Nationals.

DUP. CASE

We claim the priority from the application(s) filed in convention countries, particulars of which are as follows: **NOT APPLICABLE**

5. We state that the said invention is an improvement in or modification of the invention, the particulars of which are as follows and of which we are the applicant: **NOT APPLICABLE**

6. We state that the application is divided out of our application, the particulars of which are given below and pray that this application deemed to have been filed on ..... Under section 16 of the Act. **NOT APPLICABLE**

7. That we are the assignee or legal representatives of the true and first inventors.

8. That our address for service in India is as follows:

DR. B. VIJAYARAGHAVAN
Associate Director – Intellectual Property
Ranbaxy Laboratories Limited
Plot No.20, Sector – 18, Udyog Vihar Industrial Area,
Gurgaon - 122001 (Haryana). INDIA.
Tel. No. (91-124) 2343126, 2342001 -10; 5012501-10

9. Following declaration was given by the inventors or applicants in the convention country:

We, AJAY KUMAR SINGLA, INDERDEEP SINGH BHATIA, SANJEEV SETHI of Ranbaxy Laboratories Limited, Plot No. 20, Sector – 18, Udyog Vihar Industrial Area, Gurgaon–122001 (Haryana), India, all Indian Nationals, the true and first inventors for this invention or applicant in the convention country declare that the applicant herein, **Ranbaxy Laboratories Limited**, Corporate Office at 19, Nehru Place, New Delhi - 110 019, India, is our assignee or legal representatives.

a.

(AJAY KUMAR SINGLA)

b.

(INDERDEEP SINGH BHATIA)

c.

(SANJEEV SETHI)

10. That to the best of our knowledge, information and belief the fact and matters stated herein are correct and that there is no lawful ground of objection to the grant of patent to us on this application.

11. Followings are the attachment with the application:
    a. Provisional Specification (3 copies)
    b. Drawings (3 copies)
    c. Priority document(s)
    d. Statement and Undertaking on FORM – 3
    e. Power of Authority (Not required)
    f. Fee Rs.**3,000/-** (Rupees Three Thousand only..) in cheque bearing No. dated : drawn on

We request that a patent may be granted to us for the said invention.

Dated this **12TH** day of **November, 2003.**

For Ranbaxy Laboratories Limited

(SUSHIL KUMAR PATAWARI)
Company Secretary

FORM 2 1794 DEL 02

The Patents Act, 1970
(39 of 1970)

07 NOV 2002

COMPLETE SPECIFICATION
(See Section 10)

IBUPROFEN-CONTAINING SOFT GELATIN CAPSULES

ORIGINAL

RANBAXY LABORATORIES LIMITED
19, NEHRU PLACE, NEW DELHI - 110019

A Company incorporated under the Companies Act, 1956.

The following specification particularly describes and ascertains the nature of this invention and the manner in which it is to be performed:

The technical field of the invention relates to ibuprofen-containing soft gelatin capsules. It also relates to a pharmaceutical composition comprising a substantially clear ibuprofen solution.

The insolubility of solid drug forms in common media such as water poses a major challenge because of the resulting low bioavailability of the active ingredients. Liquid dosage forms, in contrast, generally have better bioavailability. Liquid, and especially concentrated liquid pharmaceutical compositions offer many advantages over solid compositions. Liquids are easy to swallow and provide an excellent vehicle for the uniform delivery of pharmaceutical actives. Liquids provide a rapid onset of pharmacological action, since the composition does not first have to disintegrate and dissolve in the gastrointestinal tract. Concentrated liquid compositions are ideally suited for encapsulation within a soft gelatin shell, to provide a portable and easy-to-swallow soft, flexible capsule. Encapsulation would also permit the accurate and uniform delivery of a unit dose of a pharmaceutical active, an advantage, which becomes especially important when relatively small amounts of an active are to be delivered.

Additionally, soft gelatin capsules are aesthetically appealing (especially when filled with a transparent liquid) and can be manufactured in a wide variety of sizes, shapes, and colors. Furthermore, since the dosage form is generally swallowed, it is unnecessary to flavor or otherwise mask any unpleasant taste of the active pharmaceutical ingredients. Finally unlike tablets, soft gelatin capsules do not chip or powder. A particularly good bioavailability of the pharmacologically active substance is attained if the active substance is successfully dissolved in a suitable solvent and the encapsulated solution is administered to the patient. Solutions also provide the best liquid form to obtain optimal "content uniformity" in softgel fill. In addition, a solution provides a faster and more uniform absorption of a pharmaceutical agent than a suspension. Because of these distinct technical advantages, solutions are preferred over suspensions or other dispersions.

However, despite these advantages of liquid compositions, it is not always possible to prepare a liquid composition of the desired pharmaceutical active. Many pharmaceutical actives are poorly soluble and therefore require relatively large volumes of solvent for dissolution. Also, the choice of solvents available for use in liquid compositions is limited

by safety, compatibility, stability, and economic concerns. Furthermore, the use of large volumes of solvents for solubilizing pharmaceutical actives is undesirable because, the resulting solutions would be so dilute as to require impractically large dosages for delivering a therapeutically effective amount of active, It would thus be difficult if not impossible, to encapsulate such large volumes into only one or two gelatin capsules and yet have them be of a reasonable size for easy swallowing.

One approach to overcoming these solubility problems has been to incorporate, water, water-miscible co-solvents and surfactants into the compositions. U.S. Pat. No. 4.794,117, discloses the solubilization of hydrophobic pharmaceuticals in aqueous solutions of polyethylene glycol at controlled pH; U.S. Pat. No. 4,690,823, to Lohner et al, discloses the solubilization of ibuprofen in a mixture of polyethylene glycol and a surfactant.

US patent No. 5,484,606 describes the process for reducing the precipitation of difficult to solubilize pharmaceutical actives. It uses propylene glycol to solubilize these actives along with polyethylene glycol and polyvinylpyrrolidine. US Patent No. 5,071,643 discloses a solvent system enhancing the solubility of pharmaceuticals for encapsulation. It involves use of gelling agents like sodium stearate, sodium palmitate and calcium acetate to improve solubility of pharmaceutical ingredients into polyethylene glycol.

US patent 6,287,594 discloses oral liquid compositions with improved bioavailability. These are designed to provide drugs with minimal gastric irritability wherein ratio of active drug to polymer based dispersing agent is from about 1:1 to 1:50 w/w. The resulting solution is found to be hazy.

US patent 6,387,400 discloses a process for improving concentration of a pharmaceutically active ingredient relative to fill composition. It comprises of two step process. In step one a suspension of part of a drug is made in polyethylene glycol with a molecular weight of 200 daltons to 100,000 daltons and solubilizing it subsequently with hydroxide ion. In step two remaining drug is added and resulting suspension is solubilized by adding remaining part of hydroxide ion. The ratio of a drug to fill material by weight is 1:2 and/or 5:9.

US patent 5,919,481 discloses fill material for soft gelatin capsule, which is translucent, semisolid in nature. It uses, polyalkylene glycol with average molecular weight of about 600 or less along with cellulose ether.

The US patent 5,141,961 discloses a process for solubilizing, difficulty soluble pharmaceutical actives. It uses polyethylene glycol, polyvinylpyrrolidine and monohydric alcohols. The ratio of polyethylene glycol to polyvinylpyrrolidine is about 2.5 to 1. It does not involve use of heat, solvents or surfactants.

Thus, the problem of finding an appropriate solvent system for a soft gelatin capsule fill still exists for ibuprofen. It has been difficult to achieve a soft gelatin capsule of small enough size to be acceptable to patients, i.e., small enough to swallow, while still including in that capsule a sufficient amount of ibuprofen in a clear and stable solution to provide an effective unit dose.

Summary of the invention

It is one of the aspects to provide pharmaceutical compositions comprising substantially clear solutions of ibuprofen.

It is another aspect to provide substantially clear solutions of ibuprofen comprising:

a. from about 15% to about 40% w/w of ibuprofen,
b. from about 15% to about 25% w/w of polyethylene glycol,
c. from about 20% to about 50%w/w of surfactant,
d. from about 1% to about 10% of alkalizing agent, and
e. from about 5% to about 10%w/w of water.

It is another aspect to provide soft gelatin capsules of ibuprofen providing enhanced dissolution and bioavailability of ibuprofen.

It is yet another aspect to provide a process of preparing ibuprofen containing soft-gelatin capsules comprising dispersing ibuprofen in polyethylene glycol, mixing the dispersion with

a solution of alkalizing agent in water, mixing surfactant with the dispersion to obtain a clear solution and incorporating the solution in soft gelatin capsules.

It is yet another aspect to provide a process for preparing clear solutions of ibuprofen comprising:

a. dissolving alkalizing agent in water,
b. dispersing ibuprofen in polyethylene glycol,
c. blending solution of step (a) with dispersion of step (b) with continuous stirring,
d. adding surfactant to the dispersion of step (c) and mixing to obtain a clear solution.

In one of the embodiments, the dispersion may be heated to accelerate the rate of solution.

In yet another aspect, there are provided compositions useful for relieving pain and for the treatment of inflammatory conditions.

The pharmaceutical composition may further include one or more of glucosamine, pseudoephedrine, codeine, paracetamol, econazole, hydrocodone, COX-2 inhibitors, alprazolam, dextromethorphan and chlorpheniramine. The ibuprofen and the one or more active ingredients may be combined in a single pharmaceutical composition.

Detailed description

Hydrophobic therapeutic agents, i.e., therapeutic compounds having poor solubility in aqueous solution, present problems in formulating such compounds for effective administration to patients. A well-designed formulation must, at a minimum, be capable of presenting a therapeutically effective amount of the hydrophobic compound to the desired absorption site, in an absorbable form. Even this minimal functionality is difficult to achieve when delivery of the hydrophobic therapeutic agent requires interaction with aqueous physiological environments, such as gastric fluids and intestinal fluids. Pharmaceutical compositions for delivery of such hydrophobic therapeutic agents must carry the hydrophobic compound through the aqueous environment, while maintaining the

hydrophobic compound in an absorbable form, and avoiding the use of physiologically harmful solvents or excipients.

Soft gelatin capsules or softgels are predominantly used to contain liquids wherein the active ingredients are present in the dissolved or suspended state. Solutions also provide the best liquid form to obtain optimal "content uniformity" in softgel fill. In addition, a solution provides a faster and more uniform absorption of a pharmaceutical agent than a suspension. Because of these distinct technical advantages, solutions are preferred over suspensions or other dispersions.

However, an appropriate solution of the pharmaceutical agent cannot always be achieved. Often, it is not possible to dissolve the pharmaceutical agent in a volume of solvent small enough to produce a softgel that is appropriate from the standpoint of economics and patient acceptance. Another constraint is the solvent itself. The solvent must have sufficient solvating power to dissolve a large amount of the pharmaceutical agent to produce a clear solution, and yet not hydrolyze, dissolve, or tan the softgel capsule shell.

The present invention provides clear and stable solutions of ibuprofen and the process of preparing them.

The clear and stable solutions of ibuprofen comprise:

a. from about 15% to about 40% w/w of ibuprofen,
b. from about 15% to about 25% w/w of polyethylene glycol,
c. from about 20% to about 50% w/w of surfactant,
d. from about 1% to about 10% w/w of alkalizing agent, and
e. from about 5% to about 10% w/w of water.

Polyethylene glycols generally are clear, viscous liquids or white solids, which are soluble in water and many organic solvents. The polyethylene glycols useful herein are those, which are liquids at room temperature or have a melting point slightly there above. Preferred are the polyethylene glycols having a molecular weight range from about 300 to about 1000. More preferred are the polyethylene glycols having a molecular weight range from about 400 to about 1000. Moreover, mixtures of two or more polyethylene glycols of

different average molecular weight range can also be employed in the present invention. It has been observed that, for preparing highly concentrated liquid compositions, concentrations of about 40 to about 60% w/w of polyethylene glycol are generally employed. However, in the present invention we have prepared clear solutions by employing less than 25% w/w of polyethylene glycol. Particularly, the present invention employs from about 15% to about 25% w/w of polyethylene glycol.

The composition may include at least one surfactant. Suitable surfactants can be ionic hydrophilic surfactants or non-ionic hydrophilic surfactants. The surfactant can be any surfactant suitable for use in pharmaceutical compositions. Suitable hydrophilic surfactants may be anionic, cationic, zwitterionic or non-ionic, particularly non-ionic hydrophilic surfactants. Suitable non-ionic hydrophilic surfactants include one or more of polyoxyethylene alkylethers; polyethylene glycol fatty acids esters; polyethylene glycol glycerol fatty acid esters; polyoxyethylene sorbitan fatty acid esters; polyoxyethylene-polyoxypropylene block copolymers; polyglyceryl fatty acid esters; polyoxyethylene glycerides; polyoxyethylene vegetable oils; polyoxyethylene hydrogenated vegetable oils; reaction mixtures of polyols and at least one member selected front the group consisting of fatty acids, glycerides, vegetable oil hydrogenated vegetable oils, and sterols; and mixtures thereof.

An alkalizing agent may also be added to the composition to assist in the dispersion of the ibuprofen during the formulation of the composition. Suitable alkalizing agents that are commonly used are amino acids, amino acid esters, diisopropylethylamine, ethanolamine, ethylenediamine, triethanolamine, meglumine, trimethylamine, triethylamine and triisopropanolamine. Also suitable are bases which are salts of a pharmaceutically acceptable acid, such as acetic acid, acrylic acid, adipic acid, alginic acid, alkanesulfonic acid, amino acids, ascorbic acid, benzoic acid, boric acid, butyric acid, carbonic acid, citric acid, fatty acids, formic acid, fumaric acid, gluconic acid, hydroquinosulfonic acid, isoascorbic acid, lactic acid, maleic acid, oxalic acid, para-bromophenylsulfonic acid, propionic acid, p-toluenesulfonic acid, salicylic acid, stearic acid, succinic acid, tannic acid,

tartaric acid, thioglycolic acid, toluenesulfonic acid, uric acid, and the like. Salts of polyprotic acids, such as sodium phosphate, disodium hydrogen phosphate, and sodium dihydrogen phosphate can also be used. When the base is a salt, the cation can be any convenient and pharmaceutically acceptable cation, such as ammonium, alkali metals, alkaline earth metals, and the like. Preferred cations include sodium, potassium, lithium, magnesium, calcium and ammonium. The basic amino acids can be, for example, L-arginine, L-histidine, prolamine, or mixtures thereof. The salts of pharmaceutically acceptable acids may be ammonium hydroxide, potassium hydroxide, sodium hydroxide, sodium hydrogen carbonate, aluminum hydroxide, calcium carbonate, potassium carbonate, magnesium hydroxide, magnesium aluminum silicate, synthetic aluminum silicate, magnesium aluminum hydroxide, calcium silicate or mixtures thereof.

The present solvent system in its simplest form comprises polyethylene glycol, alkalizing agent and water, the polyethylene glycol which act to dissolve the free form of the acidic agent; the alkalizing agent is present in sufficient quantity to only partially form the alkali salt of the acidic pharmaceutical agent; and the small amount of water present acts to form a solvation sphere around the acid salt permitting it to go into solution in the polyethylene glycol. Water may be present in amounts ranging from about 5% to about 10% by weight of the solution.

A process of preparing the pharmaceutical composition comprises the steps of:

a. dissolving alkalizing agent in water,
b. dispersing ibuprofen in polyethylene glycol,
c. blending solution of step (a) with dispersion of step (b) with continuous stirring,
d. adding surfactant to the dispersion of step (c) and mixing to obtain a clear solution.

Compositions of the invention are useful in relieving the pain, tenderness, inflammation (swelling) and stiffness caused by arthritis and gout. It may also be used to reduce fever

and to relieve headaches, muscle aches, menstrual pain, aches and pains from the common cold, backache, and pain after surgery or dental work.

The pharmaceutical composition may further include one or more of glucosamine, pseudoephedrine, codeine, paracetamol, econazole, hydrocodone, COX-2 inhibitors, alprazolam, dextromethorphan and chlorpheniramine. The ibuprofen and the one or more active ingredients may be combined in a single pharmaceutical composition.

The following examples illustrate various aspects of the present invention. These examples are for illustration only and should not be construed as limiting the scope of the invention.

EXAMPLES 1-3

S.no.	Ingredients	mg / capsule		
		1	2	3
1.	Ibuprofen	200.0	200.0	200.0
2.	Polyethylene glycol	178.0	163.0	142.0
3.	Polyoxyethylene sorbitan fatty acid ester	280.0	290.0	311.0
4.	Potassium carbonate	27.0	27.0	27.0
5.	Purified water	40.0	40.0	40.0
	Total	725	720	720

Process:

a. Potassium carbonate was dissolved in purified water.
b. Ibuprofen was separately dispersed in polyethylene glycol.
c. The solution of step a was blended with the dispersion of step b under constant stirring to form a dispersion.
d. To the dispersion of step c, polyoxyethylene sorbitan fatty acid ester was added and stirred until clear solution was formed.
e. The clear solution of step d was filled in soft gelatin capsules.

EXAMPLE 4

S.no.	Ingredients	mg / capsule
6.	Ibuprofen	200.0
7.	Polyethylene glycol	178.0
8.	Polyoxyethylene sorbitan fatty acid ester	280.0
9.	Meglumine	27.0
10.	Purified water	40.0
	Total	725

Process: Similar to Examples 1-3

EXAMPLE 5

S.no.	Ingredients	mg / capsule
11.	Ibuprofen	200.0
12.	Polyethylene glycol	178.0
13.	Polyoxyethylene sorbitan fatty acid ester	280.0
14.	Calcium silicate	27.0
15.	Purified water	40.0
	Total	725

Process: Similar to Examples 1-3

WE CLAIM:

1. A clear ibuprofen composition comprising:
    a. from about 15% to about 40% w/w of ibuprofen,
    b. from about 15% to about 25% w/w of polyethylene glycol,
    c. from about 20% to about 50%w/w of surfactant,
    d. from about 1% to about 5% of alkalizing agent, and
    e. from about 5% to about 10%w/w of water.
2. The composition according to claim 1 wherein ibuprofen ranges from about 15% to about 30% w/w of the composition.
3. The composition according to claim 1 wherein the polyethylene glycol has an average molecular weight ranging from about 300 to about 1000.
4. The composition according to claim 1 wherein the polyethylene glycol has a molecular weight of 400.
5. The composition according to claim 1 wherein the surfactant is a non-ionic hydrophilic surfactant.
6. The composition according to claim 5 wherein the non-ionic hydrophilic surfactant is selected from the group consisting of polyoxyethylene alkylethers; polyethylene glycol fatty acids esters; polyethylene glycol glycerol fatty acid esters; polyoxyethylene sorbitan fatty acid esters; polyoxyethylene-polyoxypropylene block copolymers; polyglyceryl fatty acid esters; polyoxyethylene glycerides; polyoxyethylene vegetable oils; polyoxyethylene hydrogenated vegetable oils.
7. The composition according to claim 6 wherein the surfactant is polyoxyethylene sorbitan fatty acid ester.

8. The composition according to claim 1 wherein the alkalizing agent is selected from the group comprising amino acids, amino acid esters, diisopropylethylamine, ethanolamine, ethylenediamine, triethanolamine, meglumine, trimethylamine, triethylamine, triisopropanolamine and salts of pharmaceutically acceptable acids.

9. The composition according to claim 8 wherein the salts of pharmaceutically acceptable acids are selected from one or more of ammonium hydroxide, potassium hydroxide, sodium hydroxide, sodium hydrogen carbonate, aluminum hydroxide, calcium carbonate, potassium carbonate, magnesium hydroxide, magnesium aluminum silicate, synthetic aluminum silicate, magnesium aluminum hydroxide and calcium silicate.

10. The composition according to claim 1, further comprising one or more active ingredients, wherein the active ingredients comprise one or more of glucosamine, pseudoephedrine, codeine, paracetamol, econazole, hydrocodone, COX-2 inhibitors, alprazolam, dextromethorphan and chlorpheniramine.

11. The composition according to claim 10 wherein ibuprofen and the one or more active ingredients are combined in a single pharmaceutical composition.

12. A soft gelatin capsule of ibuprofen, filled with a clear solution comprising:

    a. from about 15% to about 40% w/w of ibuprofen,

    b. from about 15% to about 25% w/w of polyethylene glycol,

    c. from about 20% to about 50%w/w of surfactant,

    d. from about 1% to about 5% of alkalizing agent, and

    e. from about 5% to about 10%w/w of water.

13. The soft gelatin capsule according to claim 12 wherein ibuprofen ranges from about 15% to about 30% w/w of the composition.

14. The soft gelatin capsule according to claim 12 wherein the polyethylene glycol has an average molecular weight ranging from about 300 to about 1000.

15. The soft gelatin capsule according to claim 12 wherein the polyethylene glycol has a molecular weight of 400.

16. The soft gelatin capsule according to claim 12 wherein the surfactant is a non-ionic hydrophilic surfactant.

17. The soft gelatin capsule according to claim 16 wherein the non-ionic hydrophilic surfactant is selected from the group consisting of polyoxyethylene alkylethers; polyethylene glycol fatty acids esters; polyethylene glycol glycerol fatty acid esters; polyoxyethylene sorbitan fatty acid esters; polyoxyethylene-polyoxypropylene block copolymers; polyglyceryl fatty acid esters; polyoxyethylene glycerides; polyoxyethylene vegetable oils; polyoxyethylene hydrogenated vegetable oils.

18. The soft gelatin capsule according to claim 17 wherein the surfactant is polyoxyethylene sorbitan fatty acid ester.

19. The soft gelatin capsule according to claim 12 wherein the alkalizing agent is selected from the group comprising amino acids, amino acid esters, diisopropylethylamine, ethanolamine, ethylenediamine, triethanolamine, meglumine, trimethylamine, triethylamine, triisopropanolamine and salts of pharmaceutically acceptable acids.

20. The soft gelatin capsule according to claim 19 wherein the salts of pharmaceutically acceptable acids are selected from one or more of ammonium hydroxide, potassium hydroxide, sodium hydroxide, sodium hydrogen carbonate, aluminum hydroxide, calcium carbonate, potassium carbonate, magnesium hydroxide, magnesium aluminum silicate, synthetic aluminum silicate, magnesium aluminum hydroxide and calcium silicate.

21. The soft gelatin capsule according to claim 12, further comprising one or more active ingredients, wherein the active ingredients comprise one or more of glucosamine,

pseudoephedrine, codeine, paracetamol, econazole, hydrocodone, COX-2 inhibitors, alprazolam, dextromethorphan and chlorpheniramine.

22. The soft gelatin capsule according to claim 21 wherein ibuprofen and the one or more active ingredients are combined in a single pharmaceutical composition.

23. A process of preparing a clear ibuprofen composition comprises the steps of:

a. dissolving alkalizing agent in water,

b. dispersing ibuprofen in polyethylene glycol,

c. blending solution of step (a) with dispersion of step (b) with continuous stirring,

d. optionally heating the dispersion of step (c),

e. adding surfactant to the dispersion of step (d) and mixing to obtain a clear solution.

24. The process according to claim 23 wherein ibuprofen ranges from about 15% to about 30% w/w of the composition.

25. The process according to claim 23 wherein the polyethylene glycol has an average molecular weight ranging from about 300 to about 1000.

26. The process according to claim 23 wherein the polyethylene glycol has a molecular weight of 400.

27. The process according to claim 23 wherein the surfactant is a non-ionic hydrophilic surfactant.

28. The process according to claim 27 wherein the non-ionic hydrophilic surfactant is selected from the group consisting of polyoxyethylene alkylethers; polyethylene glycol fatty acids esters; polyethylene glycol glycerol fatty acid esters; polyoxyethylene sorbitan fatty acid esters; polyoxyethylene-polyoxypropylene block copolymers; polyglyceryl fatty acid esters; polyoxyethylene glycerides; polyoxyethylene vegetable oils; polyoxyethylene hydrogenated vegetable oils.

29. The process according to claim 28 wherein the surfactant is polyoxyethylene sorbitan fatty acid ester.

30. The composition according to claim 23 wherein the alkalizing agent is selected from the group comprising amino acids, amino acid esters, diisopropylethylamine, ethanolamine, ethylenediamine, triethanolamine, meglumine, trimethylamine, triethylamine, triisopropanolamine and salts of pharmaceutically acceptable acids.

31. The composition according to claim 30 wherein the salts of pharmaceutically acceptable acids are selected from one or more of ammonium hydroxide, potassium hydroxide, sodium hydroxide, sodium hydrogen carbonate, aluminum hydroxide, calcium carbonate, potassium carbonate, magnesium hydroxide, magnesium aluminum silicate, synthetic aluminum silicate, magnesium aluminum hydroxide and calcium silicate.

32. The process according to claim 23, further comprising one or more active ingredients, wherein the active ingredients comprise one or more of glucosamine, pseudoephedrine, codeine, paracetamol, econazole, hydrocodone, COX-2 inhibitors, alprazolam, dextromethorphan and chlorpheniramine.

33. The process according to claim 32 wherein ibuprofen and the one or more active ingredients are combined in a single pharmaceutical composition.

34. A method of relieving the pain, tenderness, inflammation and stiffness caused by arthritis, gout and pains from the common cold, backache, and pain after surgery or dental work, comprising administering a clear ibuprofen composition comprising:

a. from about 15% to about 40% w/w of ibuprofen,

b. from about 15% to about 25% w/w of polyethylene glycol,

c. from about 20% to about 50%w/w of surfactant,

d. from about 1% to about 5% of alkalizing agent, and

e. from about 5% to about 10%w/w of water.

35. The method according to claim 34, further comprising one or more of glucosamine, pseudoephedrine, codeine, paracetamol, econazole, hydrocodone, COX-2 inhibitors, alprazolam, dextromethorphan and chlorpheniramine.

Dated **12TH** day of **November, 2003.**

For Ranbaxy Laboratories Limited

(Sushil Kumar Patawari)
Company Secretary

ABSTRACT

IBUPROFEN-CONTAINING SOFT GELATIN CAPSULES

The technical field of the invention relates to ibuprofen-containing soft gelatin capsules. It also relates to a pharmaceutical composition comprising a substantially clear ibuprofen solution.

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